Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

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ORIGINAL ARTICLE

Systematic reviews of convalescent plasma in COVID-19 continue to be poorly conducted and reported: a systematic review

Rebecca Whear[a,*], Alison Bethel[a], Rebecca Abbott[a], Morwenna Rogers[a], Noreen Orr[b], Sean Manzi[c], Obioha C. Ukoumunne[c], Ken Stein[a], Jo Thompson Coon[a]

[a]*Evidence Synthesis Team, National Institute for Health Research (NIHR) Applied Research Collaboration (ARC) South West Peninsula (PenARC), University of Exeter Medical School, College of Medicine and Health, University of Exeter, Exeter, Devon, UK*

[b]*Evidence Synthesis Team, University of Exeter Medical School, College of Medicine and Health, University of Exeter, Exeter, Devon, UK*

[c]*National Institute for Health Research (NIHR) Applied Research Collaboration (ARC) South West Peninsula (PenARC), University of Exeter Medical School, College of Medicine and Health, University of Exeter, Exeter, Devon, UK*

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Abstract

Objectives: To suggest possible approaches to combatting the impact of the COVID-19 infodemic to prevent research waste in future health emergencies and in everyday research and practice.

Study Design and Setting: Systematic review. The Epistemonikos database was searched in June 2021 for systematic reviews on the effectiveness of convalescent plasma for COVID-19. Two reviewers independently screened the retrieved references with disagreements resolved by discussion. Data extraction was completed by one reviewer with a proportion checked by a second. We used the Assessment of Multiple Systematic Reviews to assess the quality of conduct and reporting of included reviews.

Results: Fifty one systematic reviews are included with 193 individual studies included within the systematic reviews. There was considerable duplication of effort; multiple reviews were conducted at the same time with inconsistencies in the evidence included. The reviews were of low methodological quality, poorly reported, and did not adhere to preferred reporting items for systematic reviews and meta-analysis guidance.

Conclusion: Researchers need to conduct, appraise, interpret, and disseminate systematic reviews better. All in the research community (researchers, peer-reviewers, journal editors, funders, decision makers, clinicians, journalists, and the public) need to work together to facilitate the conduct of robust systematic reviews that are published and communicated in a timely manner, reducing research duplication and waste, increasing transparency and accessibility of all systematic reviews.

Keywords: Infodemic; Systematic review; COVID-19; Solutions; Convalescent plasma; Research waste

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* Corresponding author. St Lukes Campus, University of Exeter, 3.09 South Cloisters, Heavitree Road, Exeter EX1 2LU. Tel.: +1392 726064.

E-mail address: r.s.whear@exeter.ac.uk (R. Whear).

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What is new?

Key findings

- Duplicated systematic reviews and poor quality conduct and reporting add considerably to research waste and do not help clinical decision making.

What this adds to what is known?

- We have summarised potential ways that all those involved in funding, conducting and reporting research can help reduce research waste, ensure better research quality and improve accessibility.

What is the implication and what should change now?

- Our key messages are: STOP - Will this review make a difference?
- LOOK - look for existing reviews.
- LISTEN - listen to guidance experts and context.
- THINK. Think about limitations, innovation, and implications.
- INVEST. Invest in registries, innovation, methods, expertise, and accessible communication.

1. Introduction

The COVID-19 pandemic resulted in a substantial amount of research produced with startling speed [1,2]. While the need to understand the nature of the SARS-CoV-2 virus, its spread, impact, and possible treatments quickly was necessary, it may be argued that not all of the research was necessary and may have been of a questionable value. Indeed, Ioannides et al. (2021) concluded that the large majority of the immense and rapidly growing COVID-19 literature has been low quality [3]. Of particular concern has been the mass production of 'systematic reviews' [4,5], published at pace on similar or overlapping questions, many without recognized levels of systematic production and reporting [4,6]. This plethora of variable quality systematic reviews undermines the confidence associated with these methods and challenges the use of evidence to inform practice [7].

To propose appropriate approaches to these issues, it is essential to understand whether researchers are learning from the available evidence as it accumulates. We therefore set out to map the extent and nature of systematic reviews addressing one topic as an exemplar: the effectiveness of convalescent plasma therapy for COVID-19. Through preliminary scoping searches and previous work in this area, this topic was highlighted as a controversial area with a conflicting research history [8] and we have used it here as an example of the proliferation of research conducted on COVID-19. We conducted a preliminary search of Epistemonikos, Prospective Register of Systematic Reviews (PROSPERO), and Cochrane to see whether there were any overviews of reviews on the same topic (i.e., assessing quality of existing reviews on convalescent plasma in COVID-19) were published or underway. By exploring the timelines, characteristics, and reported methods in this body of evidence, we offer potential solutions to avoid similar research waste in the future. Specifically, we aimed to answer the following research questions:

- What is the volume, nature, and quality of systematic reviews on the effectiveness of convalescent plasma in the treatment of COVID-19?
- What is the degree of overlap between systematic reviews on the effectiveness of convalescent plasma in the treatment of COVID-19?
- To what extent are researchers learning from previously published research/reviews?

2. Methods

This review is reported as per preferred reporting items for systematic reviews and meta-analysis (PRISMA) guideline [9]. An a priori protocol was developed and registered on the PROSPERO CRD42021260124.

2.1. Information sources and search strategy

We searched the COVID-19 L·OVE repository on June 8, 2021 by using the COVID-19 Evidence link in Epistemonikos and selecting 'Systematic Reviews'. We then searched for the phrase 'convalescent plasma' within the systematic review results. The criteria for systematic reviews in the COVID-19 L·OVE repository are the same as the Epistemonikos criteria, that is, they describe an eligibility criterion, they synthesize primary studies, and they report a method that describes searching at least one electronic database. The results were exported into EndNoteX9 software.

Epistemonikos was chosen as a single resource because it collates systematic reviews from 10 major databases, including the Cochrane Database of Systematic Reviews, PubMed, Embase, and CINAHL. As such, Epistemonikos is a key resource for users of evidence providing a working dataset of systematic reviews akin to what somebody searching the literature would find. We were also keen to make the best use of an ongoing resource to identify and collate evidence rather than replicating efforts.

2.2. Eligibility criteria

2.2.1. Population

Any systematic reviews related to the effectiveness of convalescent plasma in treating COVID-19 in hospitalized patients are included. We also included any review on the use of convalescent plasma in other diseases if the authors explicitly

stated that the purpose of the review was to inform the use of convalescent plasma in the treatment of COVID-19.

2.2.2. Intervention

Any quantitative systematic review on the effectiveness of convalescent plasma in the treatment of COVID-19. We excluded review articles in which convalescent plasma was not the focus, for example, review articles which included studies on multiple therapeutic options for COVID-19.

2.2.3. Outcomes

Any systematic review that reported at least one outcome used as a measure of the effectiveness and safety of convalescent plasma for the treatment of COVID-19, for example, morbidity, mortality, time in hospital, long-term effects, need for other intervention, speed of recovery and any biological measures to determine effectiveness within the body, and safety/adverse effects. We excluded review articles which did not report on effectiveness measures.

Other eligibility criteria were that we only included systematic reviews published from December 2019 onwards and did not exclude any review based on geography, language, or quality. Systematic reviews are included on Epistemonikos (including the COVID-19 resource section) if they describe an eligibility criterion, they synthesize primary studies, and they report a method that describes searching at least one electronic database (https://www.epistemonikos.org/en/about_us/methods).

2.3. Data management

We used Endnote (*Endnote X9*) to manage retrieved records, screen references, identify, and track disagreements.

2.4. Study selection

Two reviewers (J.TC. and M.R.) independently screened the retrieved references with disagreements resolved by discussion. Reviews were excluded if they were duplicate records or were not about convalescent plasma for the treatment of COVID-19. Excluded references were checked by a third reviewer (R.W.).

2.5. Data extraction

We used a standardized data extraction spreadsheet in Excel which was piloted by the team on 10 references. Following piloting, we made changes to the spreadsheet to include further relevant details and to ensure consistent data entry throughout to help with data analysis later. One reviewer extracted data from included studies (one of A.B., R.A., R.W., M.R., N.O., and J.TC.) and another (R.A., A.B., or J.TC.) checked a proportion (20%) of the data extractions, with disagreements being discussed as a team. We extracted the following data for each systematic review: author, number of authors, date available/date of acceptance, country (of primary author), title, study design, population details, outcomes reported, funding source, whether there was a protocol and/or registration, journal, journal Impact Factor, preprint or published, whether peer-reviewed or not, whether PRISMA was cited, whether the journal required a PRISMA checklist on submission, and whether a justification for conducting the review was made. We also extracted the number of references screened, whether an information specialist was involved, whether COVID-19 resources were searched, and whether more than two terms for COVID-19 were used in the search and details relating to critical appraisal (if done and which tools). Finally, we extracted the following details relating to the included studies within each review: whether preprints were included, number/type of studies, and whether studies were COVID-19−specific or related to other pandemics.

We also extracted citation details of the primary studies included in each of the reviews and collated them in a separate Excel spreadsheet; this was conducted by one reviewer (one of A.B., R.A., R.W., M.R., N.O., and J.TC.) and checked by a second.

2.6. Critical appraisal

We used the Assessment of Multiple Systematic Reviews (AMSTAR-2) to assess the methodological quality of each review [10]. This was conducted by one reviewer and checked by two others (R.A. and O.U.). AMSTAR-2 is not designed to produce a score but to place systematic reviews into one of four quality categories (Critically Low, Low, Moderate, and High) based on seven key domains. The key domains are: (i) protocol registered before commencement of the review (item 2), (ii) adequacy of the literature search (item 4), (iii) justification for excluding individual studies (item 7), (iv) risk of bias from individual studies being included in the review (item 9), (v) appropriateness of meta-analytical methods (item 11), (vi) consideration of risk of bias when interpreting the results of the review (item 13), and (vii) assessment of presence and likely impact of publication bias (item 15). Reviews are placed into categories as follows: Critically Low—the review has more than one critical flaw and should not be relied on to provide an accurate and comprehensive summary of the available studies; Low—the review has one critical flaw and may not provide an accurate and comprehensive summary of the available studies that address the question of interest; Moderate—the systematic review has more than one weakness but no critical flaws. It may provide an accurate summary of the results of the available studies that were included in the review; and High—the systematic review provides an accurate and comprehensive summary of the results of the available studies that address the question of interest.

2.7. Analysis

We used our three research questions to structure the presentation of the results using summary tables and interactive figures to enable an overview of the evidence base.

Table 1. Percentage of reviews meeting each AMSTAR-2 criteria ($N = 51$)

AMSTAR item	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16
Yes	65	27	43	8	59	47	14	33	61	12	20	8	41	37	25	82
No	35	69	57	31	41	53	80	39	35	88	41	53	59	63	36	18
Partial	0	4	0	61	0	0	6	28	4	0	0	0	0	0	0	0
NR/No MA	-	-	-	-	-	-	-	-	-	-	39	39	-	-	39	-

Abbreviations: NR/no MA, not reported/no meta analysis.
AMSTAR-2: please find the AMSTAR 2 tool in Appendix E.

Network analysis was used to visualize and analyse the associations between the systematic reviews and the primary studies and the degree of overlap between the systematic reviews. A network is built from individual entities called nodes and the links between those entities called edges. In this analysis, the nodes of the network represent systematic reviews and primary studies and the edges in the network represent the inclusion of a primary study in a systematic review. The network metric 'degree' was then used as a measure of overlap between the systematic reviews [11]. The degree of a primary study node represents the number of systematic reviews in which the primary study is included. The inclusion of primary studies in the systematic reviews was mapped using an adjacency matrix. Using this adjacency matrix as an input, the analysis was undertaken in the Python programming language [12] using the NetworkX package [13] to calculate the node degree. Plotly Dash Cytoscape [14] was used to create the network visualization.

A Sankey diagram was constructed to visualize the links between the primary study features of publication year and study type. Again, Python [12] was used to undertake the data transformation and the package Plotly Graph Objects [15] to visualize the diagram. The unique combinations of the features, publication year, and study type were identified and then the frequency with which they occurred in the data was counted. These data enabled the unique publication year and study type combinations to be visualized with their respective weight (frequency of occurrence).

To supplement these analyses, we also extracted information on the reasons authors gave to justify undertaking their review to understand to what extent researchers are learning from previously published research/reviews.

Building on the findings, we sought and tabulated potential solutions from the literature for the issues identified and present these in the discussion. No synthesis of the outcomes relating to the effectiveness of convalescent plasma for COVID-19 is provided.

2.8. Deviations from the protocol

Due to the volume of research, we were only able to check 20% of the data extraction.

Network analysis was included as an alternative form of visualizing the data.

2.9. Patient and public involvement

There was no involvement from patients or public in the design, conduct, or reporting of our review.

3. Results

We found 102 potentially relevant reviews, which after screening, resulted in 58 included reviews. However, following data extraction, it was clear that seven of the reviews [16–22] did not meet the Epistemonikos criteria described previously (see Fig. 1 - PRISMA flow diagram). For clarity, we have excluded those reviews from the descriptions of our findings below. A list of excluded articles at full-text can be found in Appendix A.

3.1. RQ1: what is the volume, nature, and quality of systematic reviews on the effectiveness of convalescent plasma in the treatment of COVID-19?

Based on the country of the first author, the 51 reviews are conducted in China ($n = 9$), India ($n = 7$), United States ($n = 5$), Indonesia ($n = 4$), Peru ($n = 3$), Argentina ($n = 3$), United Kingdom ($n = 2$), and Germany ($n = 2$) with one review from each of the following countries Brazil, Iran, Qatar, Switzerland, Sudan, Colombia, Italy, Canada, the Netherlands, Sweden, United Arab Emirates, Australia, El Salvador, Portugal, Mexico, and Nepal.

Several reviews included studies from previous pandemics such as MERS, SARS, Ebola, and Influenza ($n = 10$) to help inform learning, but most concentrated on COVID-19–specific literature ($n = 41$). Most reviews are published

Table 2. Outcomes reported across the included systematic reviews

Outcome	Mortality	Mechanical ventilation	ICU	Hospital length of stay	Quality of life	Adverse events	Blood markers	Other
Number of reviews	46	22	14	30	3	34	24	32

Notes: ICU = days in ICU or progression to ICU, Other = clinical improvement/decline, clinical recovery, need for dialysis, disease severity, and time to recovery.

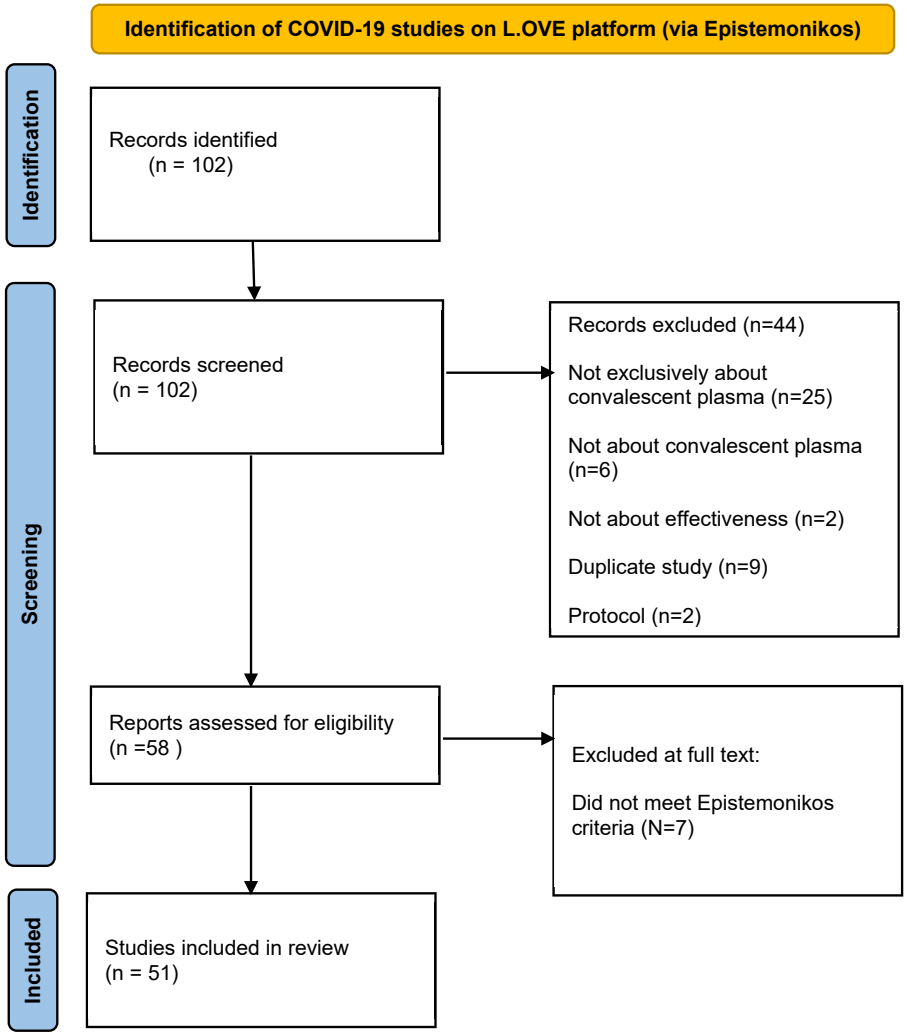

Fig. 1. PRISMA flow diagram. Adapted from: Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: An updated guideline for reporting systematic reviews. BMJ 2021; 372:n71. doi: 10.1136/bmj.n71. For more information, visit: http://www.prisma-statement.org/.

in peer-reviewed journals ($n = 38$), 10 are preprints and three are reports. Thirty five reviews are reported as systematic reviews (with or without meta-analysis), four are reported as literature reviews, two as meta-analyses, two as rapid reviews, one as a scoping review, and seven others used alternative descriptions including "living systematic review" or did not refer to themselves using any review typology. Of the 51 reviews, 32 (63%) did not report any source of funding. Of the 18 reviews that did report financial support, 8 (44%) are supported through government channels, 1 (6%) through industry, and 9 (50%) through combined government/industry/charity/education channels.

In terms of review conduct, only six of the reviews report having an information specialist involved in their search strategy. Perhaps consequently, only four reviews fully met the AMSTAR criteria for a comprehensive search strategy (31 [61%] met partial requirements). While 18 (35%) of the reviews are published in journals that overtly require a PRISMA checklist to be published, only seven of these (39%) report having a protocol and cite the PRISMA checklist with the remaining reporting no protocol. Thirty one (61%) of the reviews referenced the PRISMA checklist in their article but again 16 (52%) of these did not report having a protocol. In fact, across the entire set of included reviews, only 15 (29%) report having written a protocol. Thirty seven (73%) of the reviews report having used a critical appraisal tool to judge the quality of included studies (most commonly the Cochrane Risk of Bias tool). Full details of review characteristics can be found in Appendix B.

The vast majority of reviews, 45 (88%), are of critically low quality as per AMSTAR-2 [10] with four scoring low [23–26] and two scoring high [27,28]. Table 1 below shows the number of reviews which did or did not meet each AMSTAR-2 criteria. Notably, less than 50% of the reviews fully met AMSTAR-2 requirements on 11 criteria (codes 2, 3, 4, 6, 7, 8, 10, 11, 12, 13, 14, and 15). It is important to consider that 15 of the reviews come from low-income/middle-income countries where resources like

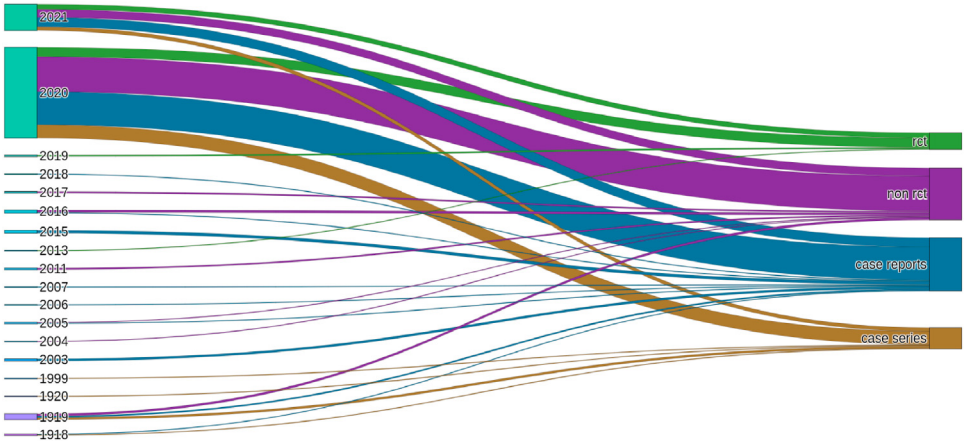

Fig. 2. Relationship between publication year and study type for all studies in the 51 systematic reviews.

access to information specialists or money for publishing in high-quality journals, for example, are more scarce.

3.2. RQ2: What is the degree of overlap between systematic reviews on the effectiveness of convalescent plasma in the treatment of COVID-19?

While all included reviews explored the effectiveness of convalescent plasma for the treatment of COVID-19, three reviews examine the effectiveness in specific populations: patients with immunodeficiency [29], areas of low resource settings [30], and effectiveness in children [31]. All of the reviews reported on similar (and sometimes numerous) outcomes to assess effectiveness. The percentage of reviews that included the most common outcomes is reported in Table 2.

There were 193 unique primary studies included in the 51 systematic reviews. The number of studies included in any one review ranged from two to 128. The primary studies were conducted between 1918 and 2021 with 35 studies published before 2020. Of the 193 studies, 23 were reported as being randomized controlled trials (RCTs), 70 were quantitative non-RCTs, 29 were case series, and 71 were case reports. Of the 51 systematic reviews, 35 included preprint publications of studies. The total number of included preprints was 31.

Figure 2 gives a pictorial impression of the number, type, and publication year of primary studies included in the 51 reviews. On the lefthand side is the year the primary study was published, each line represents one study and this line flows through to the study design blocks on the right-hand side to indicate what study types were used over the timescale on the left. As described earlier, the bulk of the studies were conducted in 2020 and 2021 and were either nonrandomized or case report study designs. This figure demonstrates that although there was an increasing amount of RCT and nonrandomized controlled trial evidence available to address this research question, case series, and case reports were still being published and included in systematic reviews, even in 2021. Please visit the interactive version here where you can follow the flow of evidence from primary studies to systematic reviews.

3.3. RQ3: To what extent are researchers learning from previously published research/reviews?

Of the 51 reviews, 82% (n = 42) report a justification for undertaking their review. The justifications ranged from there being no existing review or new primary studies to include in/update an existing review, some argue there is a clinical need or that the picture still needs clarifying or to support the search for alternative treatments particularly for low-income/middle-income countries. Of the 51 reviews, 37% (n = 19) cited previous reviews that had been conducted on this topic presumably taking them into account when deciding to undertake their own review.

The network diagram below (Fig. 3) shows the relationships between the systematic reviews and the primary studies. Systematic reviews are depicted by blue circles; the larger the circle the more primary studies included within the review. Primary studies which are highly cited within the reviews are shown toward the center of the network; less cited studies are shown around the edges of the network. Most of the primary studies are connected to only a small number of systematic reviews, with a minority of highly connected studies. This highlights the inconsistency between reviews in the nature of their included studies. You can view the interactive version of this diagram here.

Table 3 presents the number of times a primary study has been cited within one of the systematic reviews (degree value) for the 10 most commonly cited studies. The most commonly included study in a systematic review was Li et al. (2020) which was cited in 33 of the 51 systematic reviews. Two of these were RCTs, three were non-RCTs, and

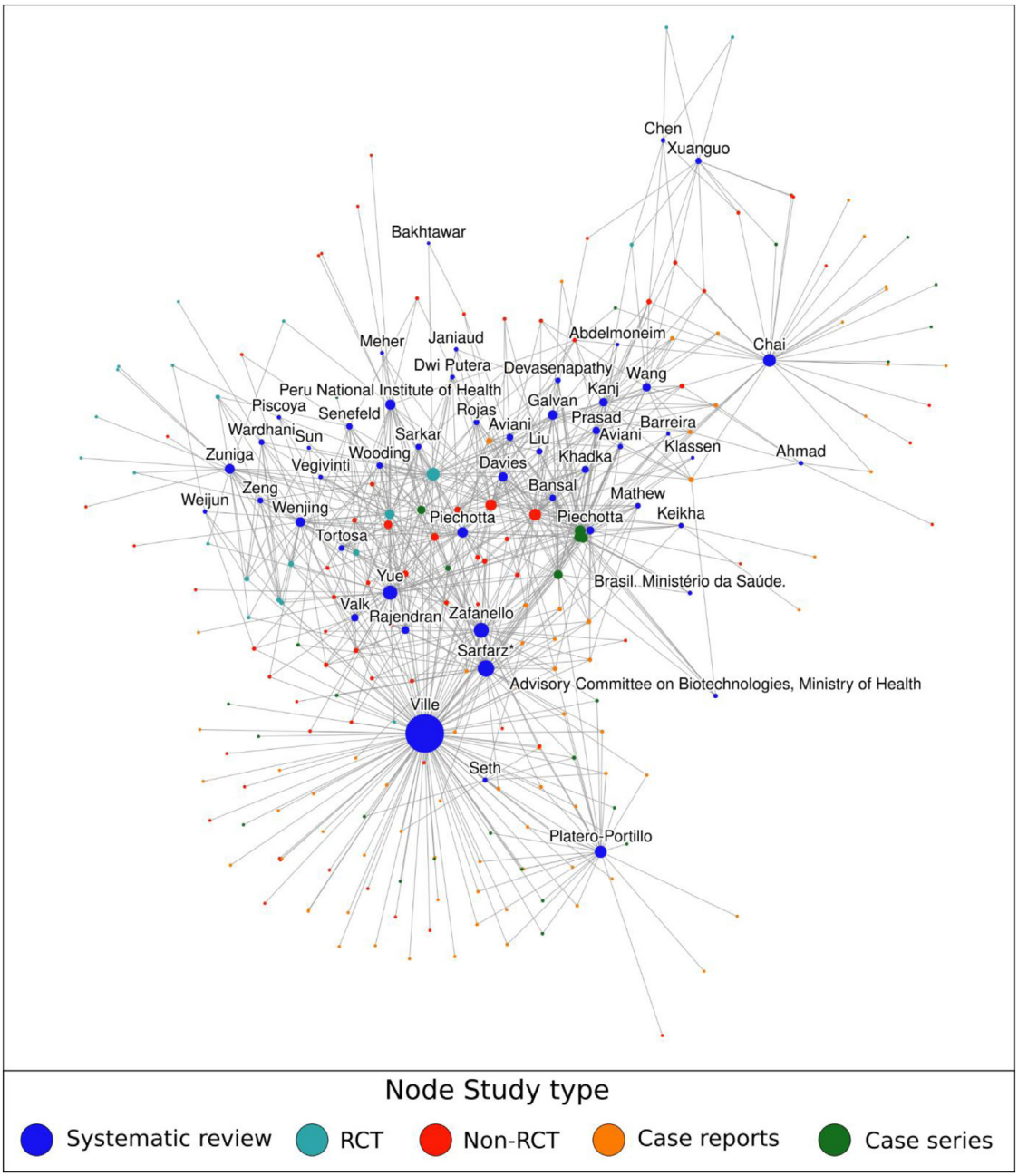

Fig. 3. Network diagram of systematic reviews and primary studies. The systematic reviews are labeled with the surname of the first author.

the remaining five were classified as case series reports (Table 3). Given that all the included systematic reviews attempted to address the same research question and published within a short time frame, we might have expected that most of the primary studies would appear in most of the systematic reviews. However, less than 25% of the primary studies were included in more than three systematic reviews indicating the reviews did not contain the same studies even if they were available. Other than for the few reviews where the research question was nuanced to a particular population ($n = 3$) or inclusion criteria were for particular study designs ($n = 5$ RCT only reviews [25,28,32–34]), it is not clear why this lack of overlap in primary studies would occur across reviews asking the same research question. The full table of degree values for the primary studies is available in Appendix C as is further information on the spread of study designs captured in reviews in Appendix D.

4. Discussion

When mapping evidence syntheses on the effectiveness of convalescent plasma therapy, we found considerable duplication of effort: 48 reviews attempting to address the

Table 3. The degree value for the 10 most commonly cited primary studies. Degree is the number of times a primary study is cited in a systematic review

Author	Year	Type	Degree value
Li et al.	2020	RCT	33
Duan et al.	2020	Non-RCT	29
Zeng et al.	2020	Non-RCT	27
Shen et al.	2020	Case series reports	26
Zhang et al.	2020	Case series reports	22
Ahn et al.	2020	Case series reports	21
Gharbharan et al.	2020	RCT	21
Ye et al.	2020	Case series reports	20
Hegerova et al.	2020	Case series reports	18
Abolghasemi et al.	2020	Non-RCT	18

same research question within 17 months with many failing to include all the available evidence, taking into account the few reviews where certain populations or eligible study designs created nuances. Furthermore, there were three times as many systematic reviews published than RCTs on the effectiveness of convalescent plasma therapy for COVID-19 within this time period. The reviews were of low methodological quality, poorly reported, and did not adhere to PRISMA guidance. Review authors failed to provide a justification for undertaking the review or cited existing published evidence. There was also scant acknowledgment of the limitations of the reviews, especially in relation to critical appraisal of the evidence and the trustworthiness of the inference on effectiveness. The impact of including preprint research, that by their nature have not been peer-reviewed, on the findings and conclusions was also rarely discussed.

The proliferation of COVID-19 research has been widely reported [35], and in particular the proliferation of low-quality systematic reviews on research questions related to COVID-19 [7]. While it is acknowledged that in a novel pandemic there is an urgent need to find answers and to find answers that are affordable and sustainable, quickly produced low-quality reviews do not necessarily add to the useful knowledge base [36]. In fact, like our fellow researchers, we argue that it creates 'noise' [7] and may add to the misinformation when authors of reviews are not transparent about the nature and robustness of the evidence they present.

We also acknowledge that there are particular issues in the context of a pandemic that make finding the best evidence difficult. In a new and rapidly developing environment the evidence is always changing and conclusions can be contradictory—depending on the evidence being used and the timing and the speed of conduct and publication. It is difficult for those searching for evidence to know where to look and to understand or assess the quality of the evidence available. However, many of these issues are ongoing problems in the research environment from its funding, conduct, publication, accessibility, and communication—the pandemic has emphasized these already-significant issues.

As part of our collective responsibility to manage misinformation (https://www.who.int/health-topics/infodemic#tab=tab_1), it is important to not only highlight the issues but also provide potential solutions/approaches to manage the infodemic.

Table 4 in Appendix F summarizes the key issues identified across the included systematic reviews and provides potential solutions from a variety of perspectives. Where possible, we provide support for these solutions with evidence or other voices. We developed this table by reflecting on what we could see in this work and from our previous work [4] regarding the problems that seem to exist in the area of evidence synthesis particularly within the context

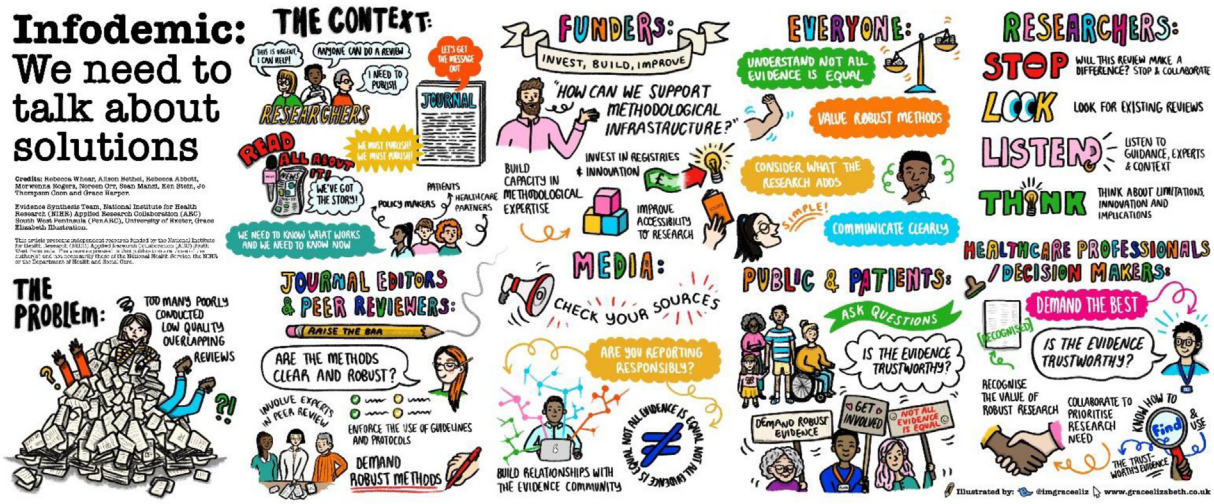

Fig. 4. Summary of the infodemic problem, context, and suggested approaches.

of a pandemic. As a team we discussed these problems and due to the continued need to work remotely we used Google Jamboard [37] to collate these together and group them into broad categories. We then began to think about potential solutions to these problems. Some of the solutions were suggested in literature that we had seen but few have evidence to support them. We found that while the problems might more neatly fit into stages, the different stages of evidence synthesis the solutions to those problems lay responsibility at the feet of all those involved in evidence synthesis—researchers, publishers/editors/peer reviewers, funders, and end users of research such as clinicians, the public, journalists, and decision makers.

We acknowledge that not all the solutions are quick fixes; it will take time to develop trust and build collaborations that share search strategies or extracted data and financial investment to develop the scope of protocol registries such as PROSPERO into a resource that can audit review progress and ensure transparency. Other solutions are more readily achievable. For example, the PRISMA reporting guidelines were developed to encourage better reporting of systematic reviews [9]. They have since been expanded to include PRISMA-S to improve reporting of search strategies [38] and PRISMA-P for reporting systematic review protocols [39]. Journals and peer reviewers can use these at the submission stage to check the adequacy of reporting and to help all reporting of systematic reviews to be more consistent and transparent. However, adherence to such guidelines is notoriously poor [40].

Our study and others [40,41] demonstrate that simply asking authors to ensure they follow these guidelines is not enough. To raise standards, journal editors need to enforce the use of relevant reporting guidelines throughout the editorial process. Ensuring the guidelines are followed [42] may mean less duplication (since the initial search, Epistemonikos now returns an additional 37 systematic reviews on convalescent plasma for COVID-19, less waste) and greater transparency and accessibility/understanding of living systematic reviews (where currently there is often a lack of clarity regarding changes that occur from one version to the next).

Similarly to our colleagues in Cochrane [43], we suggest these changes are not the responsibility of one person or even one group of people. It is the responsibility of everyone involved in the research process: researchers, funders, healthcare professionals, decision makers, journal editors, peer reviewers, patients and the public, and the broader media. To prevent repetition of the issues observed in the COVID-19 infodemic, everyone needs to understand that not all evidence is equal to value robust methods (even if they take more time), to consider what the research adds (before they conduct or replicate), and to keep all communication easy to understand and accessible. Figure 4 (Grace's summary illustration) summarizes the key messages from the potential solutions highlighted in Table 4 (Appendix F). Below we add detail to one or two key messages for each population group, but each group needs to work together to ensure changes in practice happen and are maintained.

4.1. Funders

Invest in, build, and improve methodological infrastructure and innovation such as protocol registries or accessible systematic reviewing tools and by supporting and encouraging collaboration across research groups. This will enable funders to fulfill their key role in reducing research waste and to ensure they require protocol registration and have systems to check, guide, and review protocol requirements before a systematic review can begin.

4.2. Journal editors/peer reviewers

Demand robust methods by ensuring research conduct and reporting guidelines are followed [44] and that experts are included in the process. Many have already noted the inclusion of a librarian or information specialist can improve the quality of systematic reviews [45,46], yet the majority of the reviews identified in this study did not report including this expertise in the conduct of their review. Including the appropriate professionals in both the conduct and editorial and peer-review of systematic reviews is the key [47,48].

4.3. Researchers

Stop, look, listen, and think: Researchers need to play their part in knowing/understanding how to conduct a quality systematic review. For instance, using an evidence-based approach [49−51] to thinking about whether their review is novel by seeking existing reviews before beginning, for example, by consulting purpose-made resources such as COVID-END, by considering what the review will add, following conduct and reporting guidelines, and collaborating with topic and methods experts throughout. Increasingly, researchers also need to be aware of innovations in methods and dissemination such as living systematic reviews [52] and automation (automated methods of searching, screening, or data extraction) which is building its own evidence of value [53−56] and may be able to assist in the conduct of systematic reviews, perhaps even with scarce resources, while ensuring review quality is not compromised.

4.4. Healthcare professionals/decision makers

Demand the best: we need research evidence to be relevant and trustworthy and we need to know how to find and use that trustworthy evidence. For example, reviews citing PRISMA guidelines have been reported to be of higher quality [57], as are reviews with registered protocols [58,59] and reviews that include an information specialist within the team [46]. Recognizing the value of robust

evidence and the value in collaborating to share expertise not just in the conduct of research but in the prioritization of research too.

4.5. Public and patients

Ask questions: knowing where to find robust evidence and understanding its trustworthiness is important for this group as it can facilitate conversations with their healthcare providers. But it is also important that the public and patients get involved in research (not just as participants) [60]. In doing so, they can ask questions of the research at the very beginning and help ensure the most relevant research questions are asked and helping to ensure the findings are shared in accessible ways. The Center of Excellence for Development Impact and Learning have developed a toolkit to aid researchers and policy makers in involving stakeholders with evidence and decision-making [61].

4.6. Media

Report responsibly: being aware that not all evidence is equal is key. Building relationships with the research community and checking the sources and quality of evidence can help ensure evidence is shared responsibly [36].

4.7. Strengths and limitations

Our use of Epistemonikos as a standalone resource for our searches could be seen as a strength both for being the most likely source of evidence that users of research would initially go to when searching for answers on this particular topic and for helping us to reduce research waste because we did not have to replicate searches and screening that had been done before.

A possible limitation is that while we included any reviews on the effectiveness of convalescent plasma therapy in COVID-19, there were some nuances in eligibility criteria in the reviews that might account for some of the differences in the primary studies included and we did not compare the eligibility criteria between reviews.

5. Conclusion

The COVID-19 pandemic resulted in a rapid and understandable proliferation of systematic reviews due to the urgent need for knowledge about effective and affordable treatments. It highlighted that many of the processes used for registering, conducting, and publishing systematic reviews are not fit for purpose under such circumstances. By closely examining a single research question (what is the effectiveness of convalescent plasma in the treatment of COVID-19), we have been able to identify key issues (such as proliferation and inconsistency of reviews, poor quality, overlap with but not learning from existing research) and propose ways in which the research community can help to prevent infodemics in the future.

Ultimately, as researchers we need to conduct, appraise, interpret, and disseminate systematic reviews better. It is the responsibility of all in the research community (researchers, peer-reviewers, journal editors, funders, decision makers, clinicians, journalists, and the public) to work together to facilitate robust systematic reviews that are conducted, published, and communicated in a timely manner. We welcome further thoughts and discussions on new ways to resolve these issues to help the research community move forward with positive, dynamic, and agile strategies.

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